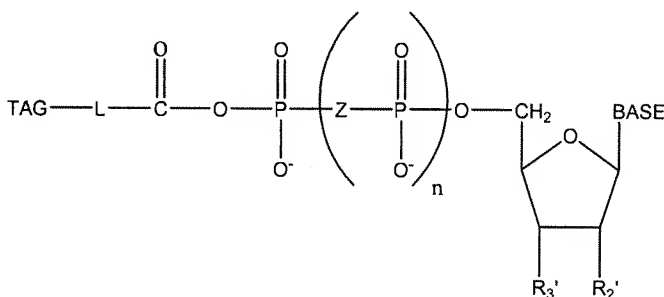


Amendments to the Claims/Listing of Claims

Please amend claims 1-19 and 27 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Withdrawn; Currently amended) **[[An]] A tagged acyl-nucleotide phosphate or phosphonate probe having according to claim 28 wherein X is a nucleotide, such that said probe has** the formula:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), =O, acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, or -(CH₂)_mOH;

R₂' and R₃' are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH, or

$-(CH_2)_m$ -phenyl where phenyl is optionally substituted with -F, -Br, -Cl, -SCH₃,
-C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃,
methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$;

n is 0-2;

m is 0 to 6; **and**

TAG₂ is a detectable label;

each Z is independently O, S, NH, or methylene;

**and L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms
selected from the group consisting of N(R), O, S or C(R)(R), wherein
said alkyl or heteroalkyl group optionally includes a carbocyclic or
heterocyclic group;**

**each R is independently H or C₁₋₆ alkyl straight or branched chain, or optionally
form an optionally substituted fused carbocyclic or heterocyclic ring
structure; and**

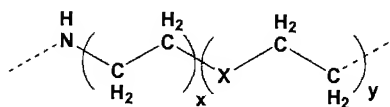
the carbonyl adjacent to L is bound to a carbon to form an acyl group;

or a pharmaceutically acceptable salt or complex thereof are as previously defined.

2. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein BASE is a purine.

3. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein BASE is a pyrimidine.

4. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, cytosine, inosine, 5-bromouracil, 5-fluorouracil, 2-aminopurine, N⁶-cyclohexyl adenine, 8-azaguanine, and 5-fluorocytosine.
5. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 4, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, and cytosine.
6. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein R₂' and R₃' are independently H or OH.
7. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein R₂' and R₃' are each OH.
8. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein L has the structure:

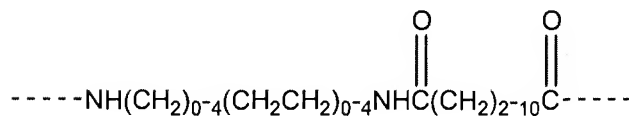
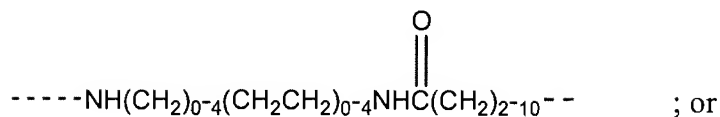
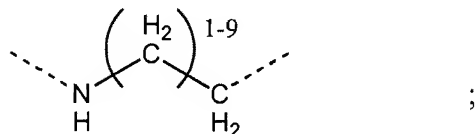


wherein

x and y are independently in the range of 0 to 4, and

X is O or CH₂.

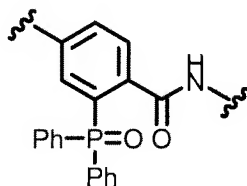
9. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein L has the structure:



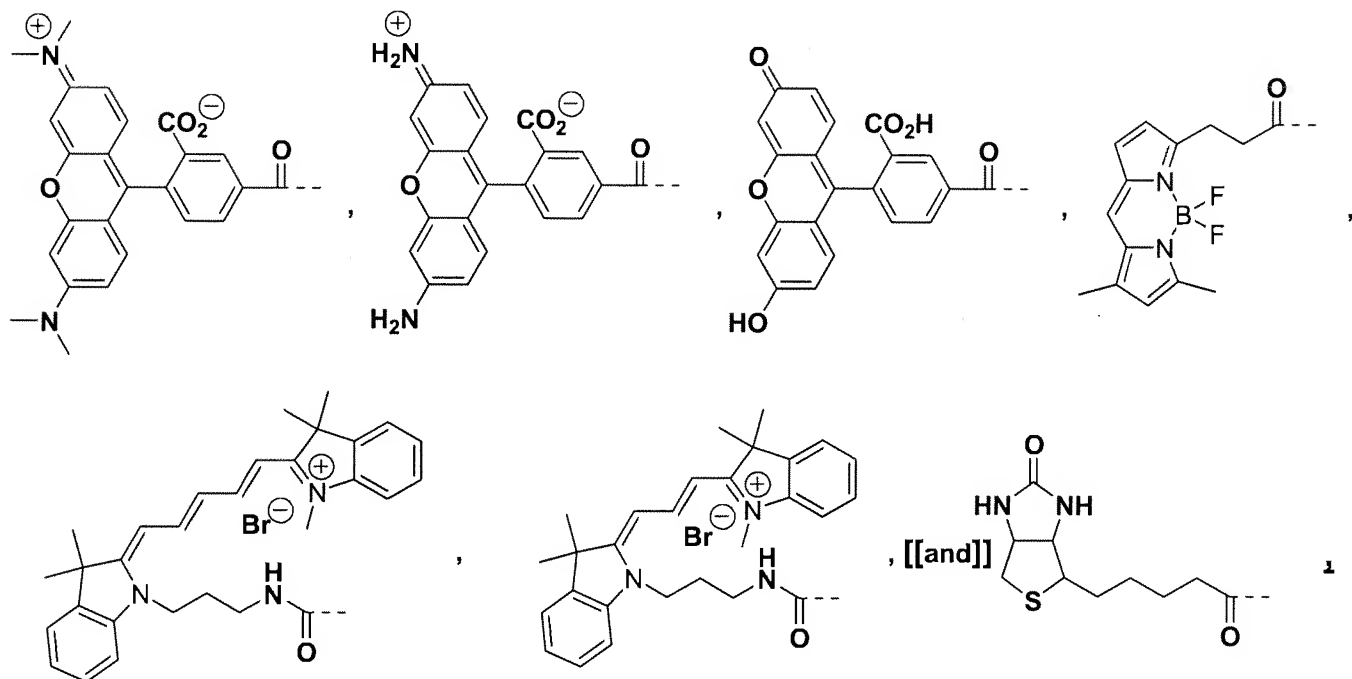
10. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 8, wherein L has the structure $\text{-NH(CH}_2\text{)}_2\text{(OCH}_2\text{CH}_2\text{)}_{1-4}\text{-}$.

11. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe according to claim 1, wherein L comprises a triazole moiety.

12. (Withdrawn; Currently amended) **[[An]] A tagged** acyl nucleotide probe according to claim 1, wherein L comprises the following moiety:

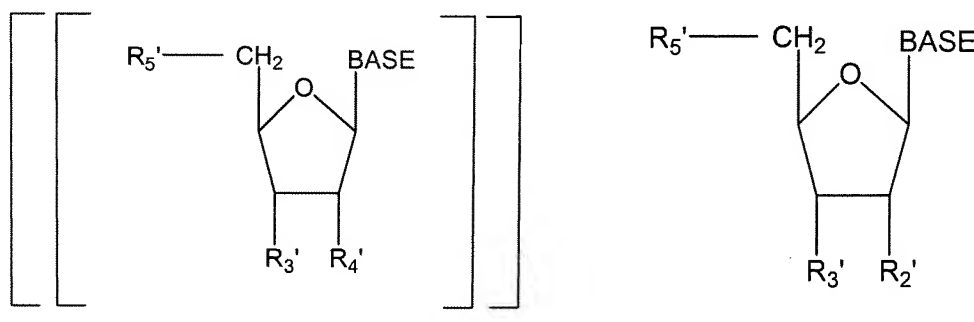


13. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe according to claim 1, wherein the TAG is selected from the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

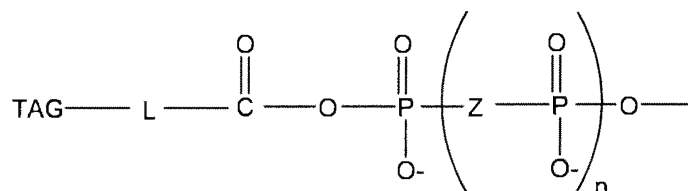
14. (Withdrawn; Currently amended) **[[An]] A tagged acyl-nucleotide phosphate or phosphonate probe having according to claim 28 wherein X is a nucleotide, such that said probe has the structure:**



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), =O, acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, or -(CH₂)_mOH;

one of R₂' and R₃' and R₅' has the following structure:



and the other two of R₂, and R₃, and R₅, are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH, or -(CH₂)_m-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, -SCH₃, -C(O)N(R)(R), -CN, -NO₂, -N(R)(R), acetoxy, -C(R)(R)(R), -OCH₃, -OCH₂CH₃, methylene dioxy, trihalomethyl, trihalomethoxy, -(CH₂)_mOH;

n is 0-2;

m is 0 to 6; and

~~TAG₁ is a detectable label;~~

~~each Z is independently O, S, NH, or methylene;~~

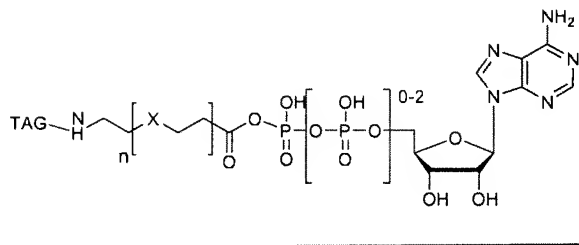
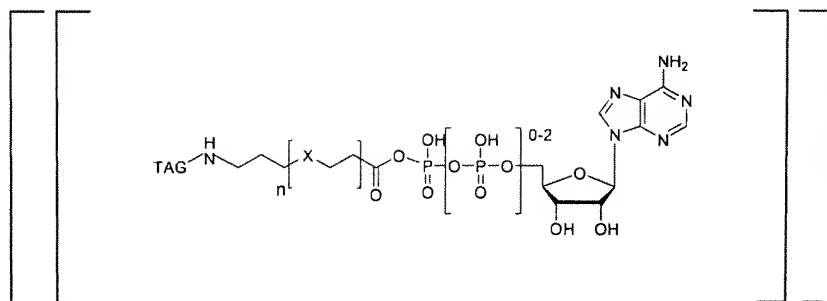
and ~~L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of N(R), O, S or C(R)(R), wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;~~

~~each R is independently H or C₁₋₆ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and~~

~~the carbonyl adjacent to L is bound to a carbon to form an acyl group;~~

~~or a pharmaceutically acceptable salt or complex thereof are as previously defined.~~

15. (Withdrawn; Currently amended) **[[An]]** **A tagged** acyl-nucleotide probe having the structure:



wherein

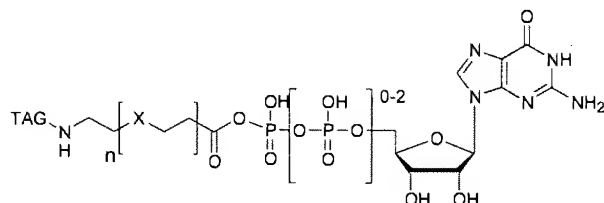
n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

16. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe having the structure:



wherein

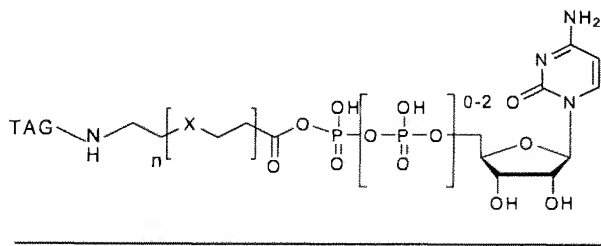
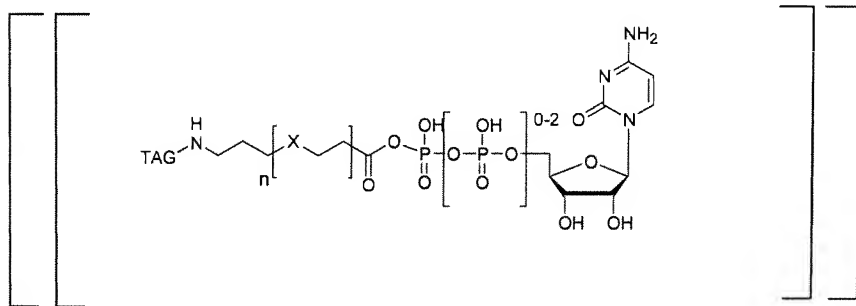
n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

17. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe having the structure:



wherein

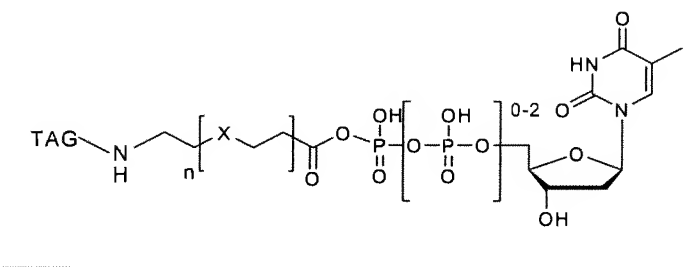
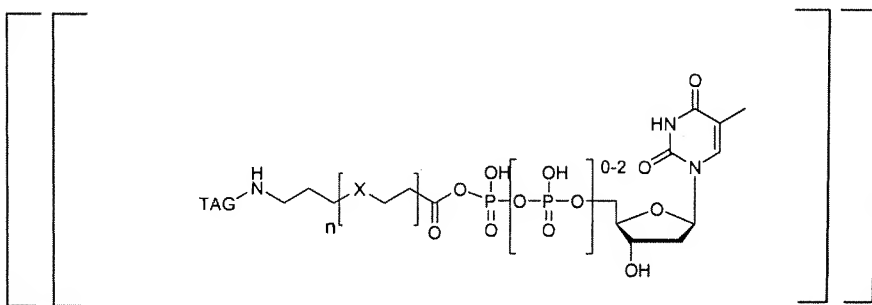
n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

18. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe having the structure:



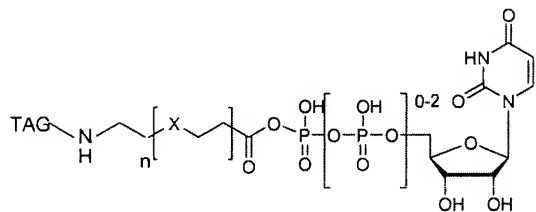
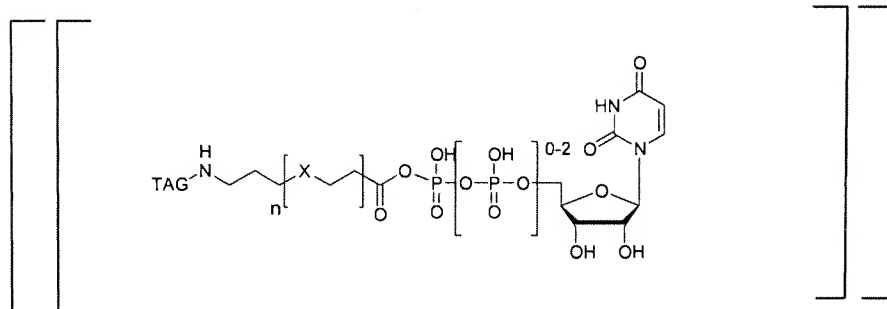
wherein

n is 1-4;

X is O or CH₂; and

TAG is a detectable label;
or a pharmaceutically acceptable salt or complex thereof.

19. (Withdrawn; Currently amended) **[[An]] A tagged** acyl-nucleotide probe having the structure:



wherein

n is 1-4;

X is O or CH₂; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

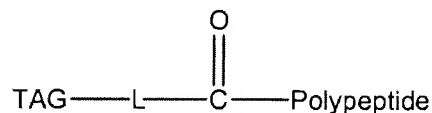
20. (Withdrawn) A method for determining the enzyme profile of one or more target proteins in a complex protein mixture, employing one or more probes comprising a nucleotide covalently bound through the terminal phosphate of a 5' mono- di- or tri-phosphate to an acyl group, which is further covalently bound to a TAG via a linker moiety "L", wherein said acyl group forms an adduct with said target protein(s) when said probe is bound to said target protein(s), said method comprising:

combining in a reaction medium said probe(s) and said complex protein mixture under conditions of reaction of said probe(s) with said nucleotide binding protein(s), whereby a conjugate of said probe(s) and said target protein(s) is formed; and determining said enzyme profile by generating a signal from one or more conjugates formed thereby;

wherein said probe(s) are selected from the nucleotide binding protein-directed probes of one of claims 1-18.

21. (Withdrawn) A method according to Claim 20, wherein said probe binds to a plurality of target proteins.

22. (Withdrawn) A composition comprising a purified labeled polypeptide having the structure:



wherein

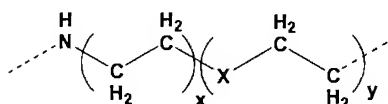
TAG is a detectable label or a solid support;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl optionally includes a carbocyclic or heterocyclic group;

the carbonyl adjacent to L is bound to a carbon to form an acyl group; and

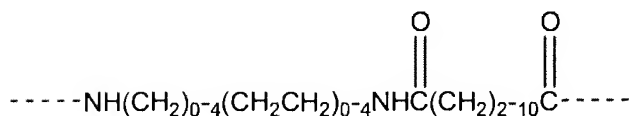
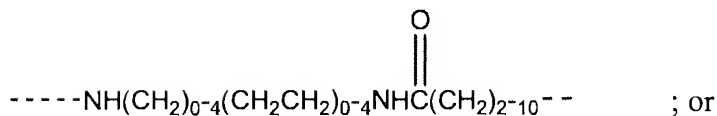
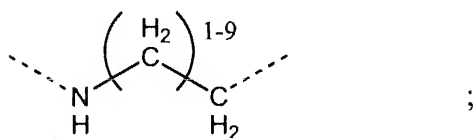
the acyl group is covalently attached through an amide, ester, or thioester linkage to a Polypeptide amino acid residue.

23. (Withdrawn) A composition according to claim 22, wherein L has the structure:



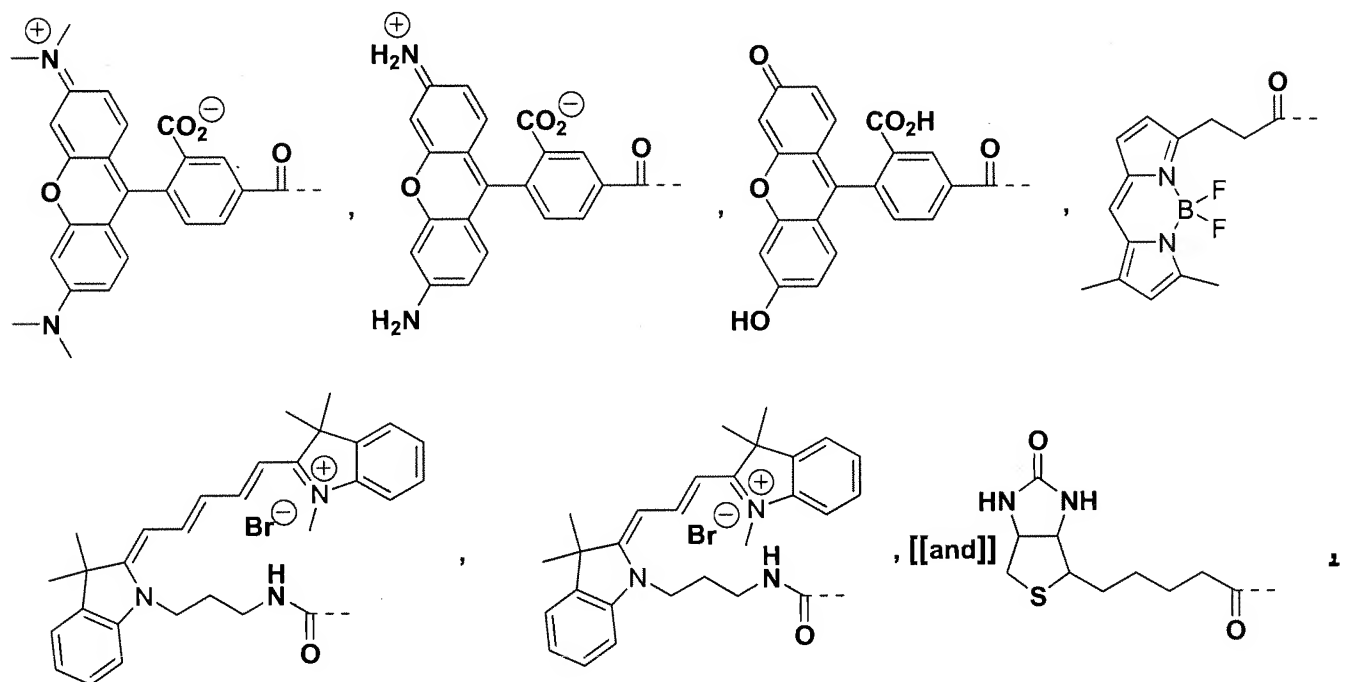
where x and y are independently in the range of 0 to 4, and X is O or CH₂.

24. (Withdrawn) A composition according to claim 22, wherein L has the structure:



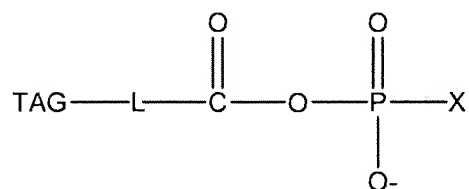
25. (Withdrawn) A composition according to claim 20, wherein L has the structure $-\text{NH}(\text{CH}_2)_2(\text{OCH}_2\text{CH}_2)_{1-4}-$.

26. (Withdrawn; Currently amended) A composition according to claim 20, wherein the TAG is selected from the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

27. (Currently amended) A tagged acyl phosphate or phosphonate probe having the formula:



wherein

X is an affinity moiety for directing the binding of said TAPP to one or more target proteins linked to the **phophate phosphate** through an oxygen or carbon;

TAG is a detectable label;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;

each R is independently H or -C₁₋₆ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and

the carbonyl adjacent to L is bound to a carbon to form an acyl group;

or a pharmaceutically acceptable salt or complex thereof.

28. (Original) The tagged acyl phosphate probe of claim 27, wherein X is selected from the group consisting of a nucleotide, nucleotide analogue, optionally substituted naphthyl group, small molecule, steroid, peptide hormone, enzyme cofactor, vitamin, enzyme substrate, lipid, prostaglandin, or receptor ligand.

29. (Withdrawn) A method of synthesizing a tagged acyl phosphate or phosphonate probe, comprising:

contacting a detectable label comprising a linking group L terminating in a carboxyl group, with a nucleotide or nucleotide analogue comprising a 5'-linked phosphate comprising an available -OH group in the presence of diisopropylcarbodiimide or isobutyl chloroformate and triethylamine to form said tagged acyl phosphate or phosphonate probe; and
purifying said probe.